

AMENDMENTS TO THE SPECIFICATION:

Please add the following at page 1, after the title and before line 1:

BACKGROUND

1. Technical Field

Please add the following at page 1, between lines 2 and 3:

2. Related Art

Please replace paragraph at page 1, beginning at line 15 with the following amended paragraph:

Various other methods of measuring characteristic fluorophore lifetimes are known, and in each case the phase shift or demodulation of a detected signal compared to an excitation signal ~~and~~ must be measured (see for example JR Lacowitz, Principles of Fluorescence Spectroscopy, Plenum Press, New York & London). However, present methods require comparatively lengthy averaging processes, which are unsuited to modern high speed processing of many measurements (for example in high throughput screening, or imaging).

Please insert the following at page 2, between lines 17 and 18:

BRIEF SUMMARY

Please replace the following paragraph at page 3, beginning at line 14:

The ~~invention~~exemplary embodiment is advantageous because it maximizes the signal emitted by the active elements of the sample, since the active elements are made to cycle substantially continuously, and thereby provide a series of quanta (the active elements are effectively saturated). A measurement of a characteristic cycle time may be made very rapidly using the invention. For example, an experimental accuracy of 1% may be obtained in a period corresponding to less than $(100 \times \text{the characteristic cycle time})^2$. This compares to conventional fluorescence lifetime measurements where illumination is pulsed, and detectors are gated and must be reset for each of a series of measurements in order to measure a lifetime. For example, the prior art method known as time correlated single photon counting generally requires an experimental duration of a few minutes.

Please replace the paragraph at page 4, beginning at line 5 as follows:

The ~~invention~~exemplary embodiment when used to measure a characteristic cycle time of a fluorophore using laser illumination, may appear superficially to resemble fluorescence correlation spectroscopy. However, there are several important differences between the invention and fluorescence correlation spectroscopy. Fluorescence correlation spectroscopy is used to determine diffusion coefficients of particles, and the detected experimental signal is caused by particles diffusing into and out of an illuminated area, the diffusion typically having a time scale of the order of milliseconds. The illumination is held at a low intensity to avoid quenching of fluorophores, and must

be stabilized to a fixed intensity to avoid introducing experimental errors due to intensity fluctuations. In contrast to this the invention measures a characteristic lifetime of a sample of fluorophores by illuminating the sample at high intensity so that it cycles substantially continuously and emits a series of photons. A measurement of the characteristic lifetime, which is typically of the order of nanosecond, may be made for example to an accuracy of 1% over a time scale corresponding to less than (100 x the characteristic lifetime)². Since the measurement may be made over such a small time duration, quenching of the sample, which will happen over a much longer duration, does not affect the measurement. Indeed, by making a series of measurements it may be possible to measure the effect of the quenching itself. There is no requirement to keep the intensity of the illumination stabilized to a particular value, provided that the intensity is sufficient to make the fluorophores of the sample cycle continuously.

Please add the following at page 9, between lines 24 and 25:

BRIEF DESCRIPTION OF THE DRAWINGS

Please add the following at page 10, between lines 14 and 15:

DETAILED DESCRIPTION OF EXEMPLARY EMBODIMENTS

Please change the title at page 41, before claim 1 as follows:

ClaimsWHAT IS CLAIMED IS: